Investigating retest effect on Logical Memory test, Trails Making test and Boston Naming test

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1 Abstract

We collected data from 15665 people across nation to investigate retest effect on three commonly used neuropsychological tests and determine whether retest effect and rate of score changes differs by diagnosis groups(normal,impaired,demented).Further,we provide a approach to adjust for retest effect for people in different diagnosis groups. We found significant difference in rate of score change between people in different groups on all three tests(i.e.logic memory test, demented vs normal(-0.27(95%CI(-0.32,-0.22)),p-value<<0.05)).Significant difference in retest effect between people in different groups on all three tests(i.e.logic memory test, impaired vs normal0.44(95% CI(0.37,0.51),p-value<<0.05)) were also found. Based on our result, we provide a approach to adjust retest effect for people in specified group by minus their score by estimated retest effect for their group.

2 Introduction

Alzheimers disease(AD) is the cause of 70-80 % dementia but it still cannot be definitively diagnosed until identification of characteristic plaques and tangles in brain after patient's death. Alzheimers disease has a severe influence on patient's life, which makes identification and treatment of Alzheimers disease highly focused. However, identification of Alzheimers disease in the living heavily depend on neuropsychological testing results. These tests measures patients dementia status and need to be taken repeatedly to measure patients' dementia status over time. Usually worse performance in these scores indicates worse dementia status but retest effect might occur in repeating these tests which yields inaccurate result of these tests. Hence, it is of great importance to investigate the retest effect on neuropsychological tests , in our analysis we focused on three commonly used tests,Logical Memory test, Trails Making test and Boston Naming test.

This analysis focuses on four aims:
1.Find out whether there is retest effect on each of three tests in our analysis and further investigate whether these effects differ by diagnosis group in first two visit of each participant.
2.Based on whole data set,quantify the rate in scores for each of three tests in our analysis and determine if within-subject rate of change over time differs by diagnosis group.
3.Whether there are retest effect in any of the diagnosis group.
4.Provide a approach to adjust for retest effect.

3 Method

3.1 Source of the Data

We collected our data from 15665 people across nation who took at least two cognitive tests and maximum twelve tests. Each person took all three tests at their visit scheduled every approximately once a year. We collected test scores for each individual in each of their visit, Logical Memory test ranges 0-25, Trails Making test ranges up to 300 and Boston Naming test ranges 0-30. Participants' demographics were recorded such as their age at baseline, sex, race and year of education. Their co-morbidities such as diabetes, history of seizures, cardiovascular disease were

also recorded.
This observational study contains numerous variables, from recent papers we found age,gender, education[1] ,smoking[2],seizures[3], stroke[4],traumatic brain injury[5] are associated with Alzheimer disease. So we decided to include them as precision variables in our model.Our response is scores for these three tests which are measures of patients' dementia status, and to measure the rate of changes for these tests , each participants' number of years between first visit and current one (visit days divided by 365) were measured. Their visit number were also recorded to measure retest effect. We chose average number of packs smoked per day as measure of smoking for participants and categorized it into two groups(packs per day >2 and packs per day <2) as an indicator of addicted smokers. We also categorized education years into two groups(education >16 and education <16) as an indicator of graduate level education. There is no paper shows strong association between remaining variables in our data and Alzheimer's disease so I didn't include remaining variables in my model.
We found some missing values among chosen covariates in our dataset,here we treat answer of "unknown"(value = 9) as missing value as well.There are 233(0.359 %) missing values for participants education years, 171(0.263 %) missing values for history of seizures, 492(0.758 %) missing values for history of traumatic brain injury, 162(0.249 %) missing values for history of stroke, 1726(3%) missing values for packs of smoke per day.There is one participant(ID 498694) who was recorded for two first visit but have different scores,I think this might be a recording error so I decided to remove this participants' data. Missing values for these covariates were minimal,so I removed them and our analysis was based on a complete base.

3.2 Statistical Models

We constructed 3 models with response from three different tests for each aim, due to limited space, we only present model for one test as a example in each case.

Model 1 :
$Test_i \sim \beta_0+\beta_1 I_{visit2i}+\beta_2 Year_i+\beta_3 dx_{1i}+\beta_4 dx_{2i}+\beta_5 I_{visit2i}*dx_{1i}+\beta_6 I_{visit2i}*dx_{2i}+\beta_7 I_{age>70i}+\beta_8 female_i+\beta_9 I_{education>16i}+\beta_{10} I_{smokei}+\beta_{11} I_{seizures\ activei}+\beta_{12} I_{seizures\ inactivei}+\beta_{13} I_{tb\ i}+\beta_{14} I_{stroke\ activei}+\beta_{15} I_{stroke\ inactivei}$

Test denotes test scores for three tests in our data(Logical Memory Test, Trails(version B), Boston Naming test).
Year denotes number of year for current visit since first visit.
dx1 is an indicator of impaired status.
dx2 is an indicator of demented status
Smoke is a indicator of smoking more than 2 packs per day
tb represents history of traumatic brain injury
Same notations will be used in for following models.

To address the first aim, we used model 1 to investigate effect of retest by testing $H0 : \beta_1 = 0$. And further investigate whether this effect differs by diagnosis group by testing $H0 : \beta_5 = \beta_6 = 0$. β_5 is the estimated difference in difference in test scores between first two visits comparing people at impaired status and normal status with all other covariate same. Since we only focused on difference between first two visit in model1, we can assume exchangeable structure between subjects. After exploratory data analysis, we found exchangeable structure was most proper structure for this model. Our result came from gee function from R package gee.

We use following two models to investigate longitudinal effect for these three tests, here I decided to include both visit number and visit year in my model. Because visit number denotes retest effect and visit year denotes decline in test scores over time. Year is a confounder when investigating retest effect where visit number is interest and visit is confounder when investigating scores changes overtime where year is interest.
Model 2:
$Test_{ij} \sim \beta_0+\beta_1 Visit_{ij}+\beta_2 Year_{ij}+\beta_3 dx_{1ij}+\beta_4 dx_{2ij}+\beta_5 Year_{ij}*dx_{1ij}+\beta_6 Year_{ij}*dx_{2ij}+\beta_7 I_{age>70i}+\beta_8 female_i+\beta_9 I_{education>16i}+\beta_{10} I_{smokei}+\beta_{11} I_{seizures\ activei}+\beta_{12} I_{seizures\ inactivei}+$

$\beta_{13}I_{tb\ i} + \beta_{14}I_{stroke\ activei} + \beta_{15}I_{stroke\ inactivei}$

Test denotes test scores(Logical Memory Test, Trails(version B), Boston Naming test) for participants.
Year denotes number of years between participants' first visit and current visit.
Visit is the visit number .

We used model 2 to address our second aim. Whole data set was used to investigate rate of score changes overtime differ in diagnosis groups .

For the second aim, we can determine the differ in rate by testing $H0 : \beta_5 = \beta_6 = 0.\beta_5$ is the difference in rate of score change comparing people under impaired dementia status and normal dementia status with all other covariates same.

Generalized estimating equations(GEE) is an excellent method to investigate longitudinal data. We can assumed different types of covariance structure of our data to get more efficient estimates. Robust variance estimator is also available for gee models for more efficient estimates. Wald test can be performed to test hypothesis we interested in. This part of our analysis was done by function gee in R package gee. After exploratory data analysis, we decided to construct a "AR-1"covariance structure gee model to address this aim.

Model 3:
$Test_{ij} \sim \beta_0 + \beta_1 Visit_{ij} + \beta_2 Year_{ij} + \beta_3 dx_{1ij} + \beta_4 dx_{2ij} + \beta_5 Visit_{ij} * dx_{1ij} + \beta_6 Visit_{ij} * dx_{2ij} + \beta_7 I_{age>70i} + \beta_8 female_i + \beta_9 I_{education>16i} + \beta_{10} I_{smokei} + \beta_{11} I_{seizures\ activei} + \beta_{12} I_{seizures\ inactivei} + \beta_{13} I_{tb\ i} + \beta_{14} I_{stroke\ activei} + \beta_{15} I_{stroke\ inactivei}$

Again, we constructed a gee model with "AR-1" covariance structure for aim 3.Here we can determine whether there are retest effect in any of diagnosis groups by testing $H0 : \beta_1 + \beta_5 = 0$ and $H0 : \beta_1 + \beta_6 = 0$.Here $\beta_1 + \beta_5$ is the estimated mean difference of retest effect comparing two subpopulations under impaired dementia status and normal dementia status with all other covariates same.

4 Results

4.1 Exploratory Data Analysis

	Normal	Impaired	Demented
Logic Memory	12.35(5.62)	10.30(4.43)	5.34(4.02)
Trails	117.30(79.08)	136.97(76.78)	202.39(88.97)
Boston Naming	25.98(5.07)	25.21(4.47)	21.33(6.81)
Age >70	28189(0.59%)	9264(0.66%)	8162(0.70%)
Age <70	19589(0.41%)	4632(0.34%)	3489(0.30%)
Female	29595(0.61%)	7149(0.51%)	5237(0.45%)
Male	18921(0.39%)	6868(0.49%)	6400(0.55%)
Education>16	17580(0.36%)	4652(0.33%)	3475(0.30%)
Education<16	31255(0.64%)	9445(0.67%)	8108(0.70%)
Packs >2	1749(0.04%)	592(0.04%)	418(0.04%)
Packs <2	41976(0.96%)	14208(0.96%)	10032(0.96%)
Seizures Recent	185(0.00%)	96(0.01%)	73(0.01%)
Seizures Remote	545(0.01%)	236(0.02%)	128(0.01%)
Seizures Absent	53955(0.99%)	9600(0.97%)	14275(0.98%)
Brain injury yes	4569(0.09%)	1593(0.11%)	1307(0.11%)
Brain injury no	46197(0.91%)	11730(0.81%)	9624(0.81%)
Stroke Recent	320(0.01%)	163(0.01v)	137(0.01%)
Stroke Remote	1165(0.02%)	551(0.04%)	528(0.05%)
Stroke Absent	31040(0.97%)	15485(0.95%)	13152(0.96%)

Table 1: Tests Scores stratified by diagnosis groups Count variable(%) Continuous variable Mean(std)

We only present exploratory data analysis results for logic memory data here. Results for other two tests are attached in appendix.

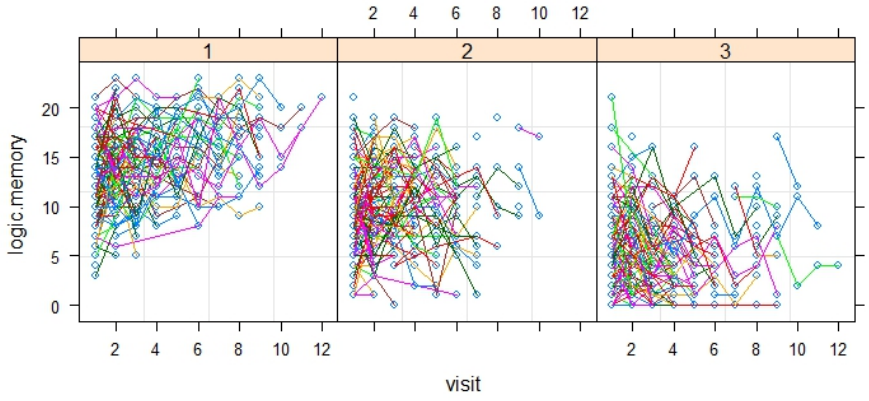

Figure 1: spaghetti plot for logic memory test(1 Normal,2 Impaired,3 Demented)

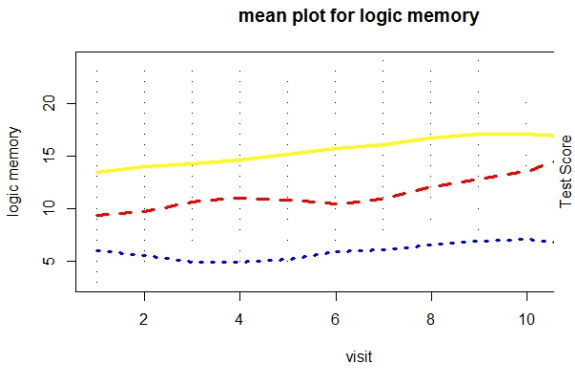

Figure 2: Mean plot for logic memory test stratified by diagnosis group(Yellow normal, Red Impaired, Blue Demented)

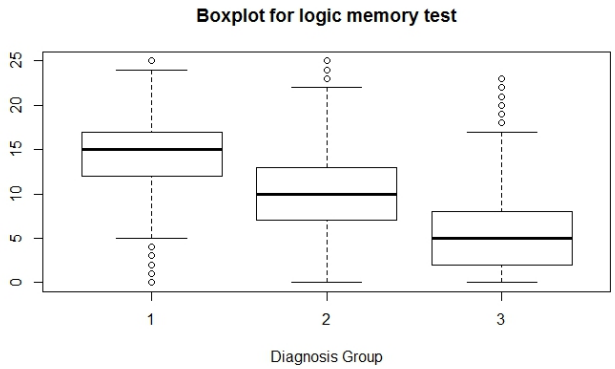

Figure 3: Boxplot for logic memory test

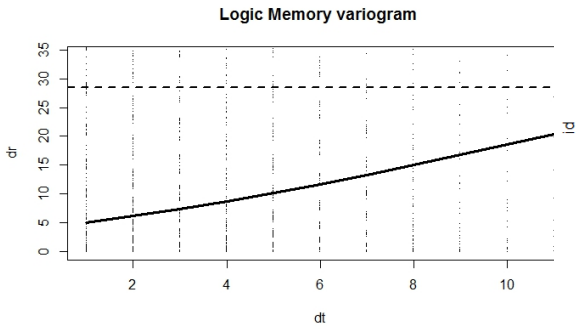

Figure 4: Variogram for logic memory test

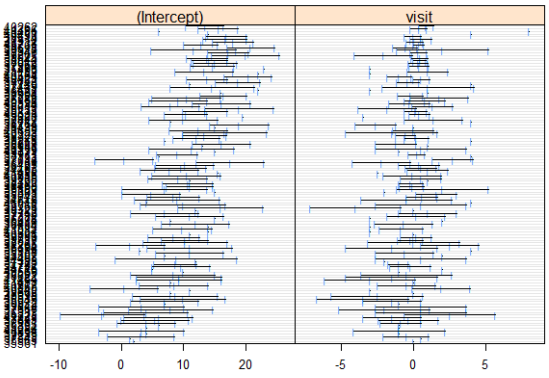

Figure 5: Individual level 95% CI

Exploratory data analysis shows for logic memory test shows that data for logic memory test has a AR-1 covariance structure because there is a obvious serial process from variogram. From spaghetti plot we can get a brief overview of trajectory for logic memory score. Stratified mean plot and boxplot shows there are obvious difference in test scores between three diagnosis groups.We found no strong influential point in this dataset, delta beta plot were presented in appendix

4.2 Statistical Inference

Results for trails (version B), Boston naming were attached in appendix due to limited space. They all get the same conclusion as logic memory test.

4.2.1 Retest effect in first two visits

	Estimate	Robust Std.	ci.low	ci.high	p-value
(Intercept)	12.73	0.08	12.58	12.88	0.00
Visit=2	0.73	0.08	0.57	0.89	0.00
Visit Year	-0.24	0.06	-0.36	-0.13	0.00
dx1	-3.39	0.07	-3.53	-3.24	0.00
dx2	-6.54	0.08	-6.70	-6.37	0.00
age.0	-1.11	0.06	-1.23	-0.99	0.00
female	0.84	0.06	0.72	0.96	0.00
educ	1.36	0.06	1.24	1.48	0.00
packyrs	0.50	0.08	0.34	0.66	0.00
tbi	0.12	0.09	-0.06	0.30	0.20
sei1	-0.11	0.43	-0.95	0.74	0.81
sei2	0.05	0.24	-0.43	0.52	0.85
stroke1	0.37	0.31	-0.23	0.98	0.23
stroke2	-0.04	0.18	-0.40	0.32	0.82
Visit=2:dx1	0.01	0.07	-0.13	0.16	0.87
Visit=2:dx2	-0.94	0.07	-1.07	-0.80	0.00

Table 2: Retest effect in first two visits for Logic Memory test

Results for logic memory test based on model1 shows that 0.73(95% CI(0.57,0.89),p-value<0.05) is the estimated retest effect between first two visits for people under normal dementia status with all other covariates same. With p-value <0.05, we can reject $H0 : \beta_1 = 0$, which implies there is significant retest effect exist in logic memory test in first two visits. 0.01(95% CI(-0.13,0.16),p-value=0.87) is estimated difference in retest effect between first two visits comparing people under normal dementia status and impaired dementia status with all other covariates same. Which implies a insignificant difference in retest effect between people under impaired status and normal status. We did a Wald test to test $H0 : \beta_5 = \beta_6$, test statistics is 120 with p-value<< 0.05, so we reject H0. There is significant difference in retest effect in impaired group and demented group .But there is no strong evidence shows that normal group and impaired group have different retest effect.

4.2.2 Quantify rate of change in scores for each of tests and determine whether this rate differs by diagnosis group

	Estimate	Robust Std	ci.low	ci.high	p-value
(Intercept)	12.00	0.08	11.84	12.16	0.00
visit	0.53	0.04	0.45	0.60	0.00
Year	-0.21	0.03	-0.27	-0.14	0.00
dx1	-2.82	0.07	-2.95	-2.70	0.00
dx2	-5.96	0.08	-6.11	-5.80	0.00
age.0	-1.29	0.06	-1.41	-1.17	0.00
female	1.03	0.06	0.91	1.15	0.00
educ	1.47	0.06	1.35	1.59	0.00
packyrs	0.51	0.14	0.23	0.79	0.00
tbi	0.13	0.09	-0.06	0.31	0.18
sei1	-0.21	0.40	-1.00	0.57	0.59
sei2	-0.01	0.25	-0.51	0.48	0.96
stroke1	-0.07	0.31	-0.68	0.54	0.82
stroke2	-0.29	0.18	-0.63	0.05	0.10
Year:dx1	0.02	0.02	-0.02	0.05	0.37
Year:dx2	-0.27	0.02	-0.32	-0.22	0.00

Table 3: Results for model 2 on logic memory test

Results for model 2 shows that there is a significant rate of changes in score of logic memory over time.-0.21(95% CI(-0.27,-0.14),p-value<<0.05) is estimated rate of change in scores of logic memory over time for people in normal diagnosis group. 0.02(95% CI(-0.02,-0.05),p-value0.37) is difference in rate of change of logic memory score between people in impaired group and normal group. We don't have enough evidence to reject $H0 : \beta_{15} = 0$.with p-value<<0.05, difference in rate between demented people and normal people is significant. Rate in changes in test scores for trails(version B) and Boston naming are significant and difference in rate by diagnosis group are significant as well.Results were attached in appendix.

	Estimate	Robust Std	ci.low	ci.high	p-value
(Intercept)	11.81	0.08	11.65	11.97	0.00
visit	0.44	0.04	0.37	0.51	0.00
Year	-0.19	0.03	-0.25	-0.12	0.00
dx1	-2.12	0.07	-2.26	-1.98	0.00
dx2	-4.65	0.09	-4.83	-4.47	0.00
age.0	-1.40	0.06	-1.52	-1.28	0.00
female	1.12	0.06	1.00	1.24	0.00
educ	1.55	0.06	1.43	1.67	0.00
packyrs	0.59	0.14	0.30	0.87	0.00
tbi	0.11	0.09	-0.07	0.30	0.24
sei1	-0.34	0.43	-1.19	0.51	0.43
sei2	-0.04	0.24	-0.52	0.44	0.88
stroke1	0.07	0.30	-0.52	0.66	0.82
stroke2	-0.36	0.17	-0.71	-0.02	0.04
visit:dx1	-0.10	0.02	-0.13	-0.06	0.00
visit:dx2	-0.40	0.02	-0.44	-0.36	0.00

Table 4: Result for model 3

Result for model 3 shows that estimated retest effect in logic memory test is 0.44(95% CI(0.37,0.51),p-value<<0.05) for people under normal dementia status.$\beta_2 + \beta_{15}$ and$\beta_2 + \beta_{16}$ are estimated retest effect for people in impaired group and demented group. We performed a Wald test for these two linear contrast and found out that they are significant(p-value <<0.05), so retest effect of logic memory test are significant in all three diagnosis groups. Estimated retest effect for normal group is 0.44, impaired group is 0.34 and demented group is 0.04, they all significantly different from each other. Result for model 3 on trails and Boston naming test shows that there exist significant retest effect in both trails and Boston naming test and these effect differ by diagnosis group significantly.Results for trails and Boston naming were attached in appendix.

4.2.3 Approaches to adjust for retest effects

From results for model 3 we saw that retest effect of logic memory test is significant in all three diagnosis groups. It is estimated that retest effect for people in normal group is 0.44, people in impaired group is 0.34, people in demented group is 0.04. So we can adjust test scores by minus visit number× estimated retest effect. Generally, we can adjust test scores for people in different diagnosis group by minus their scores by current visit number× estimated retest effect for their diagnosis group.
The limitation of this approach is we cannot adjust retest effect for people with change in their diagnosis group(i.e. normal to impaired).

5 Discussion

In this study, we investigated retest effect on three commonly used neuropsychological test(Logic Memory test, Trails (Version B)test and Boston Naming test), we are interested in retest effect and score changes over time(decline). We found that the retest effect were significant for these three tests and this effect differs in people in different diagnosis groups(normal,impaired,demented).Estimated retest effect in logic memory test is 0.44(95% CI(0.37,0.51),p-value<<0.05) for people under normal dementia status. Test scores change over time are significant as well.-0.21(95% CI(-0.27,-0.14),p-value<<0.05) is estimated rate of change in scores of logic memory over time for people in normal diagnosis group.

Based on our founding in model3, we found a approach to adjust for retest effect.we can adjust test scores for people in different diagnosis group by minus their scores by current visit number$\times$ estimated retest effect for their diagnosis group.

There are several limitations in this analysis. First, we have limited number of observations for people in impaired group demented group,which makes our estimated imprecise. Secondly, some people were included in different diagnosis groups, this might have impact on our results hence need further investigate.

There is no strong influential point in this data but there are some oddities in this data.(i.e.people clearly take two visit but have visit day 0 twice).

For future work ,we can include some potential confounder in our model for better inference and get more data for people in impaired or demented group. We need to check functional form for covariates to get a better fit of our data. We can also focus on investigating difference in retest effect in different education group or some other scientific interests.

6 Appendix

	Estimate	Robust Std	ci.low	ci.high	p-value
(Intercept)	83.23	1.18	80.91	85.54	0.00
visit 2	-4.82	1.23	-7.22	-2.42	0.00
visit year	3.80	0.93	1.98	5.62	0.00
dx1	36.05	1.13	33.84	38.26	0.00
dx2	78.96	1.60	75.82	82.10	0.00
age.0	30.21	0.98	28.29	32.14	0.00
female	4.40	1.02	2.41	6.39	0.00
educ	-21.69	0.96	-23.57	-19.80	0.00
packyrs	-5.65	1.30	-8.21	-3.10	0.00
tbi	-3.60	1.60	-6.73	-0.46	0.02
sei1	15.75	8.94	-1.78	33.28	0.08
sei2	9.73	4.35	1.19	18.26	0.03
stroke1	24.46	5.82	13.05	35.87	0.00
stroke2	23.26	3.41	16.57	29.94	0.00
visit 2:dx1	2.14	1.09	0.01	4.27	0.05
visit 2:dx2	19.10	1.35	16.45	21.75	0.00

Table 5: Retest effect in first two visits for Trails(version B) test

	Estimate	Robust Std	ci.low	ci.high	p-value
(Intercept)	27.65	0.08	27.48	27.81	0.00
visit 2	0.55	0.07	0.42	0.67	0.00
visit year	-0.27	0.05	-0.37	-0.18	0.00
dx1	-1.63	0.07	-1.76	-1.50	0.00
dx2	-3.48	0.10	-3.68	-3.28	0.00
age.0	-1.52	0.07	-1.66	-1.39	0.00
female	-0.96	0.07	-1.10	-0.82	0.00
educ	1.16	0.07	1.02	1.29	0.00
packyrs	0.49	0.09	0.32	0.66	0.00
tbi	0.41	0.11	0.20	0.62	0.00
sei1	-0.61	0.58	-1.75	0.52	0.29
sei2	-0.51	0.31	-1.11	0.09	0.09
stroke1	-0.83	0.43	-1.67	0.01	0.05
stroke2	-0.70	0.23	-1.14	-0.25	0.00
visit 2:dx1	-0.11	0.06	-0.22	-0.00	0.05
visit 2:dx2	-1.30	0.07	-1.44	-1.17	0.00

Table 6: Retest effect in first two visits for Boston Naming test

	Estimate	Robust Std	ci.low	ci.high	p-value
(Intercept)	86.60	1.26	84.12	89.08	0.00
visit	-1.70	0.62	-2.92	-0.48	0.01
Year	2.69	0.55	1.61	3.77	0.00
dx1	30.25	1.00	28.30	32.20	0.00
dx2	73.67	1.48	70.77	76.58	0.00
age.0	33.06	0.95	31.19	34.92	0.00
female	3.05	0.97	1.14	4.95	0.00
educ	-21.93	0.93	-23.76	-20.11	0.00
packyrs	-9.47	2.33	-14.05	-4.90	0.00
tbi	-3.47	1.55	-6.50	-0.44	0.02
sei1	10.58	8.34	-5.77	26.93	0.20
sei2	7.39	4.35	-1.13	15.90	0.09
stroke1	25.78	5.60	14.80	36.76	0.00
stroke2	26.98	3.25	20.61	33.36	0.00
Year:dx1	1.63	0.30	1.04	2.22	0.00
Year:dx2	5.55	0.45	4.67	6.42	0.00

Table 7: Results for model2 on Trails (Version B)test

	Estimate	Robust Std	ci.low	ci.high	p-value
(Intercept)	27.17	0.09	26.99	27.34	0.00
visit	0.18	0.04	0.11	0.25	0.00
Year	-0.14	0.03	-0.20	-0.08	0.00
dx1	-1.01	0.05	-1.12	-0.90	0.00
dx2	-2.38	0.09	-2.55	-2.20	0.00
age.0	-1.74	0.07	-1.87	-1.60	0.00
female	-0.77	0.07	-0.91	-0.63	0.00
educ	1.25	0.07	1.11	1.39	0.00
packyrs	0.48	0.16	0.16	0.80	0.00
tbi	0.36	0.11	0.14	0.57	0.00
sei1	-0.68	0.56	-1.79	0.43	0.23
sei2	-0.42	0.32	-1.05	0.21	0.19
stroke1	-0.97	0.43	-1.81	-0.12	0.03
stroke2	-0.92	0.23	-1.37	-0.47	0.00
Year:dx1	-0.06	0.01	-0.09	-0.04	0.00
Year:dx2	-0.45	0.03	-0.50	-0.40	0.00

Table 8: Results for model2 on Boston Naming test

	Estimate	Robust Std	ci.low	ci.high	p-value
(Intercept)	87.80	1.26	85.32	90.27	0.00
visit	-3.11	0.63	-4.35	-1.88	0.00
Year	3.97	0.56	2.87	5.07	0.00
dx1	28.29	1.22	25.90	30.67	0.00
dx2	68.36	1.80	64.83	71.88	0.00
age.0	33.13	0.95	31.26	34.99	0.00
female	3.10	0.97	1.20	5.01	0.00
educ	-21.91	0.93	-23.73	-20.09	0.00
packyrs	-9.45	2.34	-14.03	-4.87	0.00
tbi	-3.46	1.54	-6.48	-0.43	0.03
sei1	10.59	8.35	-5.77	26.96	0.20
sei2	7.38	4.34	-1.13	15.89	0.09
stroke1	25.67	5.61	14.68	36.66	0.00
stroke2	27.02	3.25	20.65	33.40	0.00
visit:dx1	1.88	0.34	1.22	2.55	0.00
visit:dx2	5.96	0.50	4.98	6.95	0.00

Table 9: Results for model 3 on Trails(version B)test

	Estimate	Robust Std	ci.low	ci.high	p-value
(Intercept)	27.10	0.09	26.92	27.27	0.00
visit	0.28	0.04	0.21	0.35	0.00
Year	-0.23	0.03	-0.29	-0.17	0.00
dx1	-0.95	0.06	-1.08	-0.83	0.00
dx2	-1.99	0.11	-2.20	-1.77	0.00
age.0	-1.74	0.07	-1.88	-1.60	0.00
female	-0.78	0.07	-0.92	-0.64	0.00
educ	1.25	0.07	1.11	1.38	0.00
packyrs	0.47	0.16	0.15	0.80	0.00
tbi	0.36	0.11	0.14	0.57	0.00
sei1	-0.68	0.56	-1.78	0.43	0.23
sei2	-0.42	0.32	-1.04	0.21	0.19
stroke1	-0.96	0.43	-1.80	-0.11	0.03
stroke2	-0.92	0.23	-1.37	-0.47	0.00
visit:dx1	-0.07	0.02	-0.10	-0.04	0.00
visit:dx2	-0.48	0.03	-0.54	-0.41	0.00

Table 10: Results for model 3 on Boston Naming test

	visit 1	visit 2	visit 3	visit 4	visit 5	visit 6	visit 7	visit 8	visit 9	visit 10	visit 11	visit 12
visit 1	1.00	0.79	0.77	0.74	0.71	0.68	0.65	0.61	0.59	0.56	0.57	0.58
visit 2	0.00	1.00	0.82	0.80	0.76	0.73	0.69	0.67	0.66	0.62	0.62	0.71
visit 3	0.00	0.00	1.00	0.83	0.80	0.77	0.74	0.72	0.68	0.64	0.66	0.61
visit 4	0.00	0.00	0.00	1.00	0.84	0.81	0.78	0.76	0.72	0.63	0.67	0.69
visit 5	0.00	0.00	0.00	0.00	1.00	0.84	0.81	0.79	0.78	0.71	0.70	0.67
visit 6	0.00	0.00	0.00	0.00	0.00	1.00	0.84	0.81	0.79	0.72	0.72	0.71
visit 7	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.83	0.82	0.75	0.75	0.77
visit 8	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.85	0.80	0.77	0.76
visit 9	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.83	0.76	0.75
visit 10	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.85	0.83
visit 11	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.88
visit 12	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00

Table 11: Empirical Covariance estimates for logic memory

	visit 1	visit 2	visit 3	visit 4	visit 5	visit 6	visit 7	visit 8	visit 9	visit 10	visit 11	visit 12
visit 1	1.00	0.79	0.75	0.71	0.69	0.64	0.62	0.62	0.61	0.51	0.42	0.25
visit 2	0.00	1.00	0.80	0.75	0.71	0.68	0.65	0.64	0.63	0.54	0.43	0.28
visit 3	0.00	0.00	1.00	0.81	0.78	0.71	0.68	0.68	0.65	0.52	0.34	0.15
visit 4	0.00	0.00	0.00	1.00	0.81	0.74	0.72	0.69	0.68	0.58	0.61	0.39
visit 5	0.00	0.00	0.00	0.00	1.00	0.81	0.76	0.75	0.72	0.57	0.51	0.34
visit 6	0.00	0.00	0.00	0.00	0.00	1.00	0.78	0.76	0.72	0.64	0.53	0.22
visit 7	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.80	0.75	0.64	0.60	0.56
visit 8	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.79	0.67	0.66	0.36
visit 9	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.72	0.56	0.19
visit 10	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.74	0.23
visit 11	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.63
visit 12	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00

Table 12: Empirical Covariance estimates for Trails(Version B)

	visit 1	visit 2	visit 3	visit 4	visit 5	visit 6	visit 7	visit 8	visit 9	visit 10	visit 11	visit 12
visit 1	1.00	0.86	0.82	0.79	0.76	0.72	0.70	0.69	0.69	0.66	0.57	0.58
visit 2	0.00	1.00	0.86	0.82	0.78	0.74	0.71	0.68	0.68	0.69	0.62	0.51
visit 3	0.00	0.00	1.00	0.88	0.85	0.81	0.77	0.74	0.75	0.64	0.45	0.51
visit 4	0.00	0.00	0.00	1.00	0.89	0.84	0.81	0.80	0.78	0.74	0.65	0.53
visit 5	0.00	0.00	0.00	0.00	1.00	0.89	0.85	0.81	0.81	0.72	0.67	0.52
visit 6	0.00	0.00	0.00	0.00	0.00	1.00	0.88	0.84	0.82	0.76	0.72	0.68
visit 7	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.86	0.84	0.76	0.67	0.49
visit 8	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.88	0.77	0.53	0.67
visit 9	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.85	0.67	0.38
visit 10	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.81	0.74
visit 11	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.69
visit 12	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00

Table 13: Empirical Covariance estimates for Boston Naming

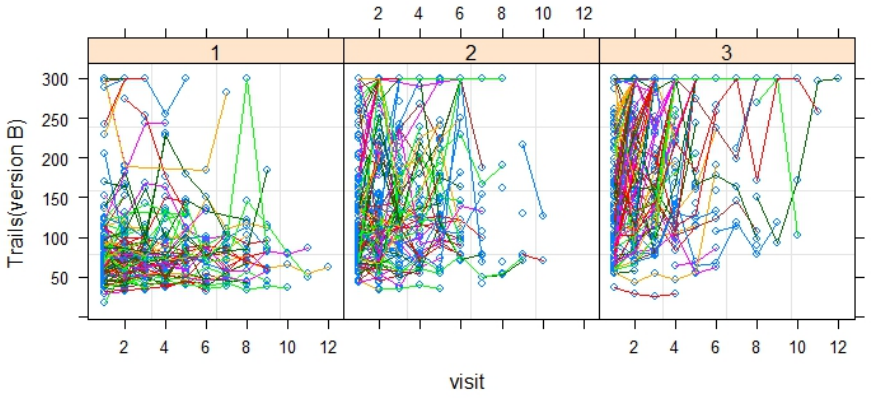

Figure 6: spaghetti plot for Trails (version B) test

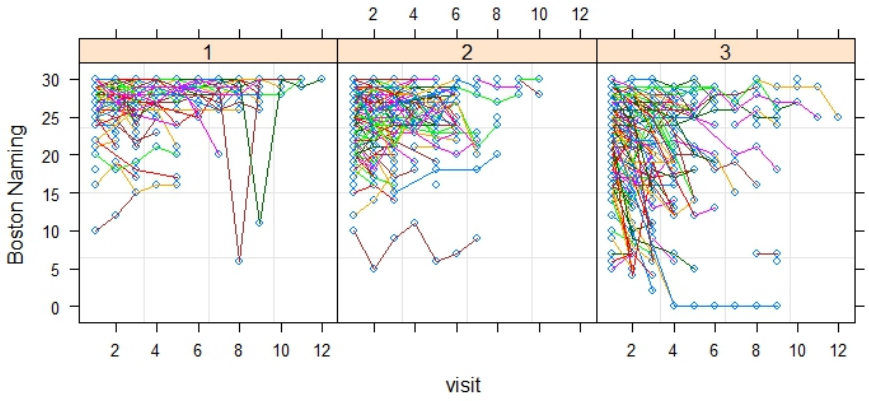

Figure 7: spaghetti plot for Boston Naming test

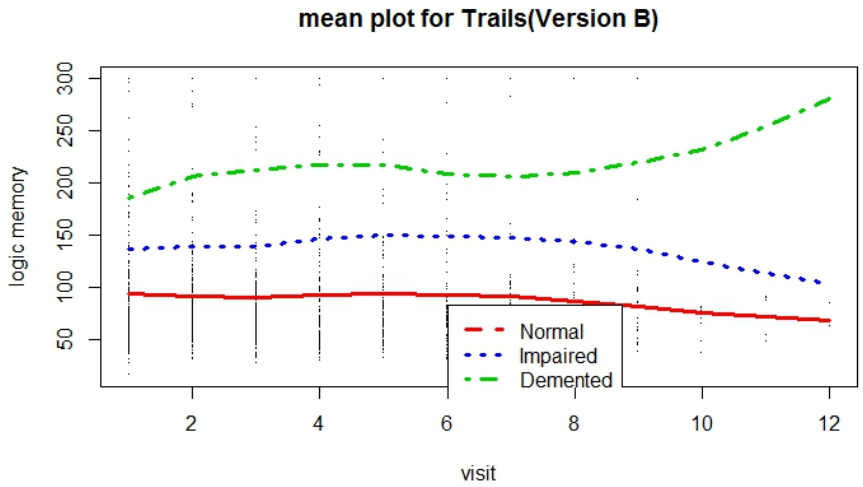

Figure 8: Mean plot for Trails test

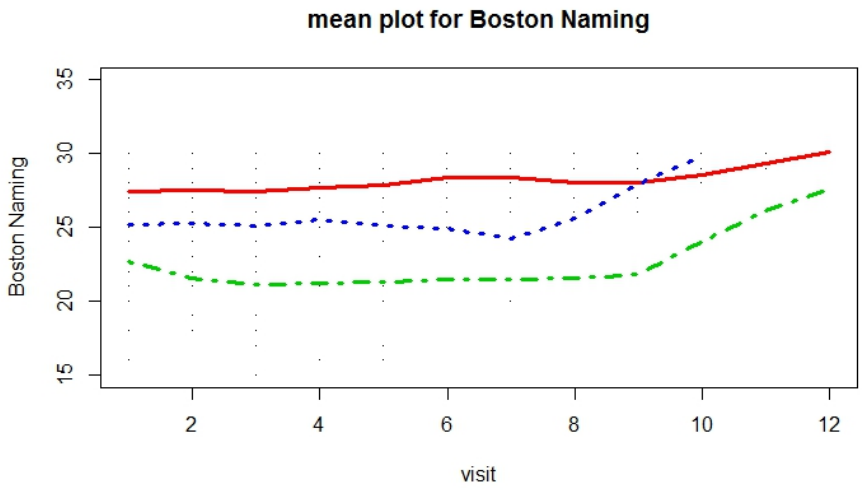

Figure 9: Mean plot for Boston Naming test

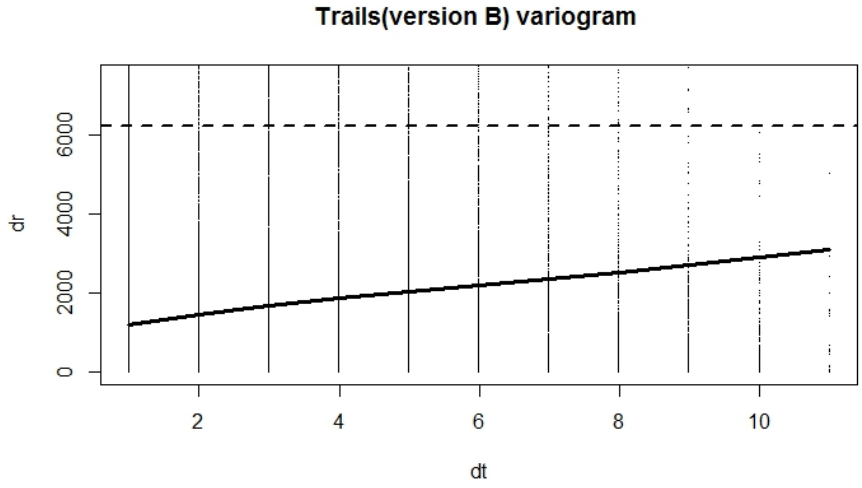

Figure 10: Variogram for Trails test

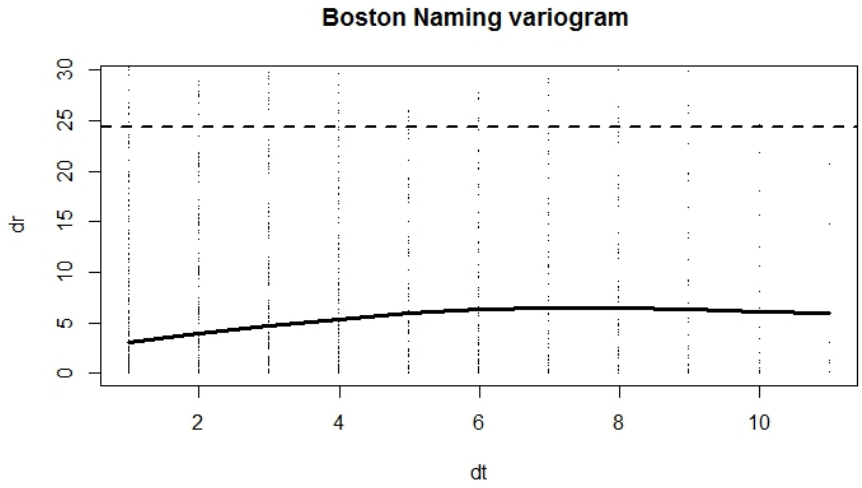

Figure 11: Variogram for Boston Naming test

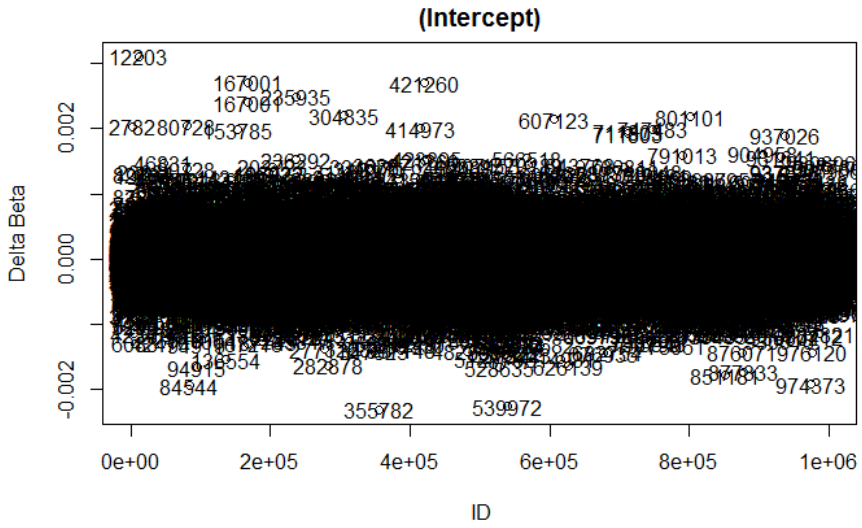

Figure 12: Delta Beta

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